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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,950	03/27/2001	Paul M. Guyre	DC-0153	4097

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,950	GUYRE ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/03/05 has been entered.

Claims 1-3 are pending.

In view of the amendment filed 08/03/05 , the following rejection remains:

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coligan et al. (Current Protocols in Immunology, Greene Publishing Associates and Wiley-Interscience, New York, 1991; pages 2.1.1-2.1.3, 2.1.9-2.1.11, and 2.1.17-2.1.22) in view of U.S. Patent 5,077,216, Zwadlo et al (IDS Reference BA) Zwadlo et al (IDS Reference AX) and newly cited Hogger et al(Pharmaceutical Research, 1998, Vol.15, pages 296-302) as is evidenced by Sulahian et al (Cytokine, 2000, Vol.12, pages 1312-1321).

Applicant's arguments filed 08/03/05 have been fully considered but they are not persuasive.

Applicant asserts that : (i) none of the references teach that CD163 is useful for monitoring an early signaling event, i.e. within the first 1-12 hours in an inflammatory response cascade in a patient; (ii) Zwadlo et al. teaches away from the present invention in teaching that the RM3/1 antigen (i.e. CD163) is appearing in blood at 24 and 72 hours after exposure to the inflammatory stimulus, thus there is no motivation for the skilled artisan to modify the teaching in the art to monitor CD163 levels before 24 hours after exposure to the inflammatory stimulus, (iii) In view of teaching of Arondel et al., one of skill in the art could not reasonably extrapolate the levels of CD163 at 1 to 12 hours after exposure to an inflammatory stimulus based upon the teaching of Zwaldo et al.

Coligan et al., teach an antibody-sandwich ELISA to detect soluble antigens, which is the most useful of the immunosorbent assays for detecting antigen because it is very sensitive (see page 2.1.9 in particular), plates are coated with a specific capture antibody, test samples added, and soluble antigens are detected with another antibody. A developing reagent is adted to detect antibody/antigen complexes (see page 2.1.0 in particular). Coligan et al. teach that ELISAS are useful for screening biological fluids (e.g. from plasma) for antigen content (see page 2.1.20, left column in particular).

Coligan et al. to not teach a method for detecting an early signaling event in an inflammatory response, comprising detecting CD163 with antibodies directed against CD163, wherein said antibody is monoclonal antibodies MAC2-158, or MAC2-48.

The US Patent '216 teaches a method of detecting a p155 human mononuclear phagocyte-specific antigen using the monoclonal antibodies MAC2-158 and MAC2-48 (see columns 1, 7, 12, ant the claims in particular). The monocytes detected were obtained from human plasma (see column 5, paragraphs 1-2 in particular).

Zwaldo et al. (IDS Reference BA) teach that RM3/1 antigen (.i.e. CD161 antigen) is useful for monitoring an early signaling event in an inflammatory response in a patient. The examiner disagree with Applicant interpretation that Zwadlo et al. teaches away from the present invention in teaching that the RM3/1 antigen (i.e. CD163) is appearing late in the inflammatory response. Zwaldo et al. teach that the levels of RM3/1 antigen (i.e. CD163) reached a maximum levels late in the inflammatory response. However, Applicants attention is drawn to pages 299, 301 and 303, wherein Zwaldo et al. explicitly teach that depending on the stage of inflammation RM3/1 antigen is expressed at different levels. Zwaldo et al. explicitly teach that in acute inflammation , i.e. early in an inflammatory response, RM3/1 antigen expressed to varying degree, depending on the stage of inflammation. In addition, Zwaldo et al. ., (IDS Reference AX teach to monitor the appearance of RM3/1 positive macrophages in blood between 24 and 72 hr post inflammatory response (see abstract in particular).

It would be immediately obvious to one skill in the art that Zwaldo et al., teach that detection of the expression of RM3/1, i.e. CD163 is useful for monitoring an early signaling event in an inflammatory response. Moreover, as is evidenced by Sulahian et al., based on the

teaching of Zwaldo et al., it has been suggested that CD163 bright macrophages play a role in the resolution of inflammation as they are found in the high numbers in inflammation tissues. It is noted that applicants are co-authors of Sulahian et al., reference.

Moreover, the examiner disagreed with Applicant's interpretation of Arondel et al. reference. The is no teaching in said references that early signaling events in an inflammatory response cascade can not be extrapolated by measuring protein levels at 0 and at 24 hr or later. Arondel et al. monitor the balance of the expression levels between two different signals, i.e. inductive and inhibitory signals of inflammation. Arondel et al., teach that in addition to higher expression of IL1, M90T also caused a decrease in expression of IL-1ra, at 4 hr after infection, that at 8 hr p.i. was caught up probably due to massive recruitment of producing cells in infected zone. , thereby restoring IL-1/Il-1ra balance. However, it is noted that Arondel et al., teaching is irrelevant for the instant application, since the instant claims do not recite measuring the ration between inductive and inhibitory signals.

Hogger et al., teach that injection of glucocorticoids into primates or human volunteers results in an increase of RM3/1 positive blood monocytes within 6 hr. Hogger et al., also teach that monocytes expressing RM3/1 antigen i.e. CD163, are also present in acute inflammation (see entire document, page 296 in particular). Hogger et al., teach that the level of expression of RM3/1 antigen i.e. CD163, can be measured by antibody labeling and subsequent FACS analysis (see page 302 in particular). In other words, it would be immediately obvious to one skill in the art that Hogger et al., teach that expression of RM3/1 antigen i.e. CD163 is an indicative of an early signaling event in the inflammatory response.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the MAC2-158 or MAC2-48 antibodies as capture antibodies taught by the '216 patent and the antibodies taught by Zwaldo et al., as the detection antibody in the ELISA assay taught by Coligan et al. to have a method for monitoring the course of an inflammatory condition or inflammatory response in a patient by detecting the levels of CD163 in the biological sample as taught by Zwaldo and Hogger et al.

One of ordinary skill in the art would have been motivated to use the antibodies taught by the '216 patent and Zwaldo et al. in the ELISA taught by Coligan et al. because to detect and monitor the presence of CD163 in a biological sample, such as human plasma, during an early inflammatory condition/process, such as rheumatoid arthritis by detecting CD163 (i.e. RM3/1 antigen) as taught by Zwaldo et al and Hogger et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because detecting CD163 levels can be used to monitor an early inflammatory response cascade in the patient, as taught by Zwaldo et al and Hogger et al. . CD163 levels in biological sample can be detected using the antibodies taught by the '216 patent and Zwaldo et al. in the ELISA taught by Coligan et al.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The following new ground of rejection are necessitated by the amendment filed 08/03/05

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5 Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" determining whether there is a detectable elevation in the level of CD163 within 1 to 12 hours of exposure to the inflammatory stimulus indicative of an early signaling event..." claimed in 1 represent a departure from the specification and the claims as originally filed. The specification and the claims as originally field only support " demonstrating that elevation in the level of CD163 within 1 to 12 hours acts as an early signaling event in the inflammatory response".

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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October 14, 2005